

Epidemiology of coronary heart disease in women

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The male excess in coronary heart disease (CHD) is well recognised. Nevertheless, CHD is the leading cause of death in women as well as men in most industrialised countries.^{1–4} In the United Kingdom in 2002, coronary heart disease accounted for approximately 64 000 (22%) of the 288 000 deaths or one in five deaths in men, and 53 000 (17%) of the 318 000 deaths, or one in six death in women at all ages.^{1–3}

CHD MORTALITY RATES, INTERNATIONAL COMPARISONS AND TIME TRENDS

Table 1 shows mortality rates for CHD by age and sex in the United Kingdom and also the ratio in men compared to women. The male excess for CHD is most pronounced at younger ages but still apparent throughout life. Age standardised CHD mortality rates by sex for selected countries between 1999–2000 are shown in fig 1,^{2,3} illustrating enormous international variations. The highest documented rates are now seen in countries in Eastern Europe with women in these countries having over 10-fold the rates of women in Japan. A male excess in CHD is evident in all countries; nevertheless, the CHD rates in men and women internationally correlate strongly. Time trends for selected countries from 1969 to 2001,^{2,3} shown in fig 2 illustrate different patterns in these countries. Both the United States and United Kingdom have had notable declines in CHD rates in three decades. In contrast, CHD rates in women in Eastern European countries such as the Ukraine, or developing countries such as Mauritius, have increased over a similar time period. The profound temporal trends indicate that the major determinants of mortality rates are likely to be potentially modifiable environmental factors rather than genetic susceptibility.

CORONARY HEART DISEASE RISK FACTORS

Numerous factors have been implicated in the aetiology of CHD.⁴ Of these, the role of the classical risk blood cholesterol concentrations, blood pressure and cigarette smoking have been the best documented in both men and women. Mean levels of these risk factors increase with age, more steeply in women than in men. At younger ages, women tend to have lower mean levels of systolic blood pressure and serum cholesterol compared to men; this pattern reverses at older ages. In contrast, cigarette smoking habit appears to decline with age in both men and women. Though the prevalence of smoking is higher in older men, the most recent figures show higher prevalence of smoking in younger women compared to men.^{3,5}

The evidence for the major importance of raised blood cholesterol for CHD in both men and women is overwhelming. Raised blood pressure, fibrinogen values, cigarette smoking habit, diabetes, inflammatory markers such as C-reactive protein, and obesity are also well documented risk factors in women. Of these, reduction of blood pressure and cholesterol have been demonstrated to be of cardiovascular benefit in randomised trials which have included women.⁶ The classical risk factors—blood pressure, raised blood

Table 1 Coronary heart disease mortality rates by sex and age group and ratio of CHD mortality in men compared to women in the United Kingdom 2002^{2,4}

	Age group (years)				
	45–54	55–64	65–74	75–84	85+
Death rates/100000					
Women	19	79	235	864	2342
Men	93	271	579	1540	3257
Ratio men: women	4.9	3.4	2.5	1.8	1.4

cholesterol and cigarette smoking—appear to confer the same relative increase in CHD risk in women and some of the sex difference in CHD can be explained by lower levels of risk factors in women, at least at younger ages. In particular, cigarette smoking habit has been substantially lower in the past in women compared to men, but trends appear to be reversing in younger cohorts. Some of the apparent protection that women seem to have from CHD may diminish as prevalence of cigarette smoking in women increases and even exceeds that in men.

While the magnitude of the relative risk of subsequent CHD associated with the major risk factors are similar in men and women, the absolute risk of CHD is higher in men compared to women at any given level of risk factor.^{7,8} This has implications for individual-based preventive therapies such as pharmacologic treatment of hypertension and hypercholesterolaemia. Though trials indicate these confer similar relative benefits for CHD in men and women, the absolute benefit is likely to be lower in women. Thus, the risk-benefit balance may be different and more finely balanced in women compared to men when individual preventive treatments are considered.

Lifestyle factors, diet, physical activity, and psychosocial factors in CHD may have effects through influencing levels of known physiological risk factors such as lipid values and blood pressure or through other mechanisms involved such as inflammation or thrombosis. Though there are few randomised trials of primary prevention of CHD using lifestyle measures in women, it may seem reasonable to assume from the consistency in the data from observational studies that similar lifestyle factors apply to women as well as men. Observational studies in women as well as men indicate lower CHD rates are associated with dietary patterns with lower saturated fat intake, higher fruit and vegetable intake and higher physical activity levels.⁶

SEX HORMONES

Despite obvious differences in concentrations of endogenous sex hormone, the assumption that women have less CHD than men because either high oestrogen concentrations are protective or high testosterone concentrations are adverse for CHD is not well supported by available evidence. This evidence

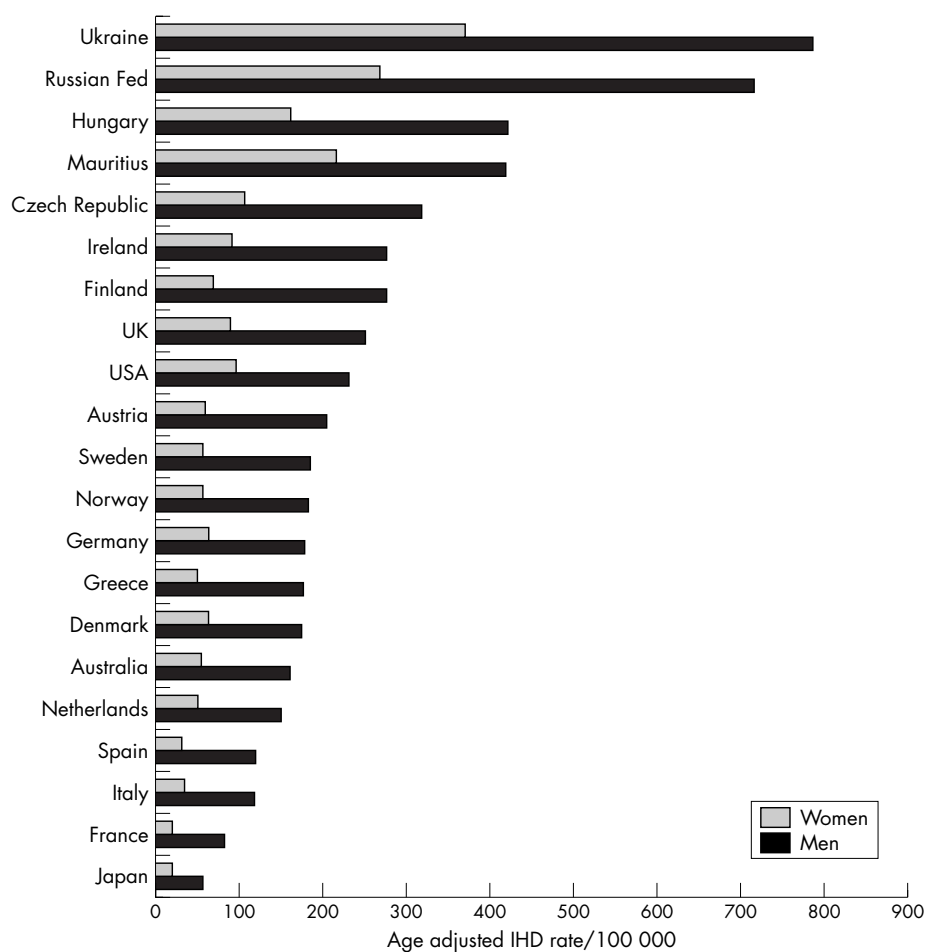


Figure 1 Age adjusted coronary heart disease rates for men and women aged 35-74 years in selected countries, 1999-2000.^{4,5}

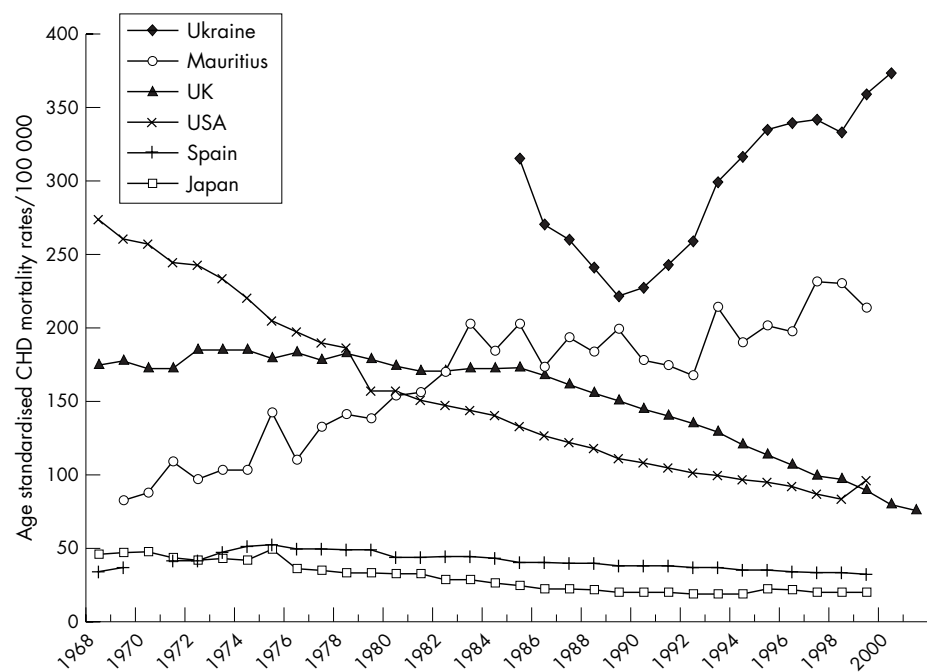


Figure 2 Trends in age adjusted coronary heart disease mortality rates for men and women aged 35-74 years in selected countries, 1968-2001.^{4,5}

is derived from either observational studies of endogenous hormone values or from more recent postmenopausal hormone replacement therapy trials such as the Women's Health Initiative, which showed no benefits for CHD with oestrogen supplementation with or without progestogen.^{9–12}

CONCLUSIONS

The international variations and time trends in CHD rates in women indicate that a substantial proportion of CHD in women can be prevented. Rates in women closely correlate with rates in men, suggesting that the environmental and lifestyle factors that lead to high CHD rates in men also lead to high rates in women. Population based approaches which aim to modify lifestyle factors such as diet, smoking and physical activity are likely to benefit both men and women. The observation that women in countries with high CHD rates have over sixfold the rates in men living in countries with low CHD rates indicates that environmental influences far outweigh the impact of any biologic differences between men and women in CHD susceptibility. Though women have lower CHD rates than men, CHD is the leading cause of mortality in women as well as men in most industrialised countries. Preventive interventions need to be targeted at women as well as men.

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REFERENCES

- 1 **Office for National Statistics.** *Mortality statistics: DHI Series no. 34 2001 and Series DH2 no. 29.* London: Office for National Statistics, 2002.
- 2 **World Health Organization.** *Statistical information (WHOSIS).* Geneva: WHO, 2004.
- 3 **Petersen S, Peto V, Rayner M.** *Coronary heart disease statistics 2004.* London: British Heart Foundation, 2004.
- 4 **Marmot M, Elliott P, eds.** *Coronary heart disease epidemiology.* Oxford: Oxford University Press, 1997.
- 5 **Health Survey for England 2002.** <http://www.publications.doh.gov.uk/stats/trends1.htm>.
- 6 **Mosca L, Appel LJ, Benjamin EJ, et al.** Evidence based guidelines for cardiovascular disease prevention in women. *Circulation* 2004;**109**:672–93.
- 7 **Isles CG, Hole DJ, Hawthorne VM, et al.** Relation between coronary risk and coronary mortality in women of the Renfrew and Paisley survey: comparison with men. *Lancet* 1992;**339**:702–6.
- 8 **Khaw KT, Rose G.** Cholesterol screening programmes: how much benefit? *BMJ* 1989;**299**:606–7.
- 9 **Barrett-Connor E, Goodman-Gruen D.** Prospective study of endogenous sex hormones and fatal cardiovascular disease in postmenopausal women. *BMJ* 1995;**311**:1193–6.
- 10 **Wu FC, von Eckardstein A.** Androgens and coronary artery disease. *Endocr Rev* 2003;**24**:183–217.
- 11 **Rossouw JE, Anderson GL, Prentice RL, et al for the Writing Group for the Women's Health Initiative Investigators.** Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the women's health initiative randomized controlled trial. *JAMA* 2002;**288**:321–33.
- 12 **Anderson GL, Limacher M, Assaf AR, et al for the Women's Health Initiative Steering Committee.** Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: the women's health initiative randomized controlled trial. *JAMA* 2004;**291**:1701–12.